#6

Fig. 1A

```
AGCTTCCGAG AGGCAGCCGA TGTGAGCATG TGCGCACAGA TTCGTCTCCC AATGGCATGG        60

CAGCTTCAAG GAAAATTATT TTGAACAGAC TTGAATGCAT AAGATTAAAG TTAAAGCAGA       120

AGTGAGAACA AGAAAGCAAA GAGCAGACTC TTTCAACTGA GAATGAATAT TTTGAAGCCC       180

AAGATTTTAA AGTGATGATG ATTAGAGTCG TACCTAAAAG AGACTAAAAA CTCCATGTCA       240

AGCTCTGGAC TTGTGACATT TACTCACAGC AGGCATGGCA ATTTTAGCCT CACAACTTTC       300

AGACAGATAA AGACTTGGAG GAAATAACTG AGACGACTCC CTGACCCAGG AGGTTAAATC       360

AATTCAGGGG GACACTGGAA TTCTCCTGCC AGC ATG GTG AAC TCC ACC CAC CGT       414
                                     Met Val Asn Ser Thr His Arg
                                      1               5

GGG ATG CAC ACT TCT CTG CAC CTC TGG AAC CGC AGC AGT TAC AGA CTG         462
Gly Met His Thr Ser Leu His Leu Trp Asn Arg Ser Ser Tyr Arg Leu
         10                  15                  20

CAC AGC AAT GCC AGT GAG TCC CTT GGA AAA GGC TAC TCT GAT GGA GGG         510
His Ser Asn Ala Ser Glu Ser Leu Gly Lys Gly Tyr Ser Asp Gly Gly
     25                  30                  35

TGC TAC GAG CAA CTT TTT GTC TCT CCT GAG GTG TTT GTG ACT CTG GGT         558
Cys Tyr Glu Gln Leu Phe Val Ser Pro Glu Val Phe Val Thr Leu Gly
 40                  45                  50                  55

GTG ATC AGC TTG TTG GAG AAT ATC TTA GTG ATT GTG GCA ATA GCC AAG         606
Val Ile Ser Leu Leu Glu Asn Ile Leu Val Ile Val Ala Ile Ala Lys
                 60                  65                  70

AAC AAG AAT CTG CAT TCA CCC ATG TAC TTT TTC ATC TGC AGC TTG GCT         654
Asn Lys Asn Leu His Ser Pro Met Tyr Phe Phe Ile Cys Ser Leu Ala
             75                  80                  85

GTG GCT GAT ATG CTG GTG AGC GTT TCA AAT GGA TCA GAA ACC ATT ATC         702
Val Ala Asp Met Leu Val Ser Val Ser Asn Gly Ser Glu Thr Ile Ile
         90                  95                 100

ATC ACC CTA TTA AAC AGT ACA GAT ACG GAT GCA CAG AGT TTC ACA GTG         750
Ile Thr Leu Leu Asn Ser Thr Asp Thr Asp Ala Gln Ser Phe Thr Val
    105                 110                 115

AAT ATT GAT AAT GTC ATT GAC TCG GTG ATC TGT AGC TCC TTG CTT GCA         798
Asn Ile Asp Asn Val Ile Asp Ser Val Ile Cys Ser Ser Leu Leu Ala
120                 125                 130                 135

TCC ATT TGC AGC CTG CTT TCA ATT GCA GTG GAC AGG TAC TTT ACT ATC         846
Ser Ile Cys Ser Leu Leu Ser Ile Ala Val Asp Arg Tyr Phe Thr Ile
                140                 145                 150

TTC TAT GCT CTC CAG TAC CAT AAC ATT ATG ACA GTT AAG CGG GTT GGG         894
Phe Tyr Ala Leu Gln Tyr His Asn Ile Met Thr Val Lys Arg Val Gly
            155                 160                 165

ATC AGC ATA AGT TGT ATC TGG GCA GCT TGC ACG GTT TCA GGC ATT TTG         942
Ile Ser Ile Ser Cys Ile Trp Ala Ala Cys Thr Val Ser Gly Ile Leu
        170                 175                 180
```

Fig. 1B

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TTC ATC ATT TAC TCA GAT AGT AGT GCT GTC ATC ATC TGC CTC ATC ACC      990
Phe Ile Ile Tyr Ser Asp Ser Ser Ala Val Ile Ile Cys Leu Ile Thr
    185                 190                 195

ATG TTC TTC ACC ATG CTG GCT CTC ATG GCT TCT CTC TAT GTC CAC CTG     1038
Met Phe Phe Thr Met Leu Ala Leu Met Ala Ser Leu Tyr Val His Leu
200                 205                 210                 215

TTC CTG ATG GCC AGG CTT CAC ATT AAG AGG ATT GCT GTC CTC CCC GGC     1086
Phe Leu Met Ala Arg Leu His Ile Lys Arg Ile Ala Val Leu Pro Gly
                220                 225                 230

ACT GGT GCC ATC CGC CAA GGT GCC AAT ATG AAG GGA GCG ATT ACC TTG     1134
Thr Gly Ala Ile Arg Gln Gly Ala Asn Met Lys Gly Ala Ile Thr Leu
            235                 240                 245

ACC ATC CTG ATT GGC GTC TTT GTT GTC TGC TGG GCC CCA TTC TTC CTC     1182
Thr Ile Leu Ile Gly Val Phe Val Val Cys Trp Ala Pro Phe Phe Leu
        250                 255                 260

CAC TTA ATA TTC TAC ATC TCT TGT CCT CAG AAT CCA TAT TGT GTG TGC     1230
His Leu Ile Phe Tyr Ile Ser Cys Pro Gln Asn Pro Tyr Cys Val Cys
    265                 270                 275

TTC ATG TCT CAC TTT AAC TTG TAT CTC ATA CTG ATC ATG TGT AAT TCA     1278
Phe Met Ser His Phe Asn Leu Tyr Leu Ile Leu Ile Met Cys Asn Ser
280                 285                 290                 295

ATC ATC GAT CCT CTG ATT TAT GCA CTC CGG AGT CAA GAA CTG AGG AAA     1326
Ile Ile Asp Pro Leu Ile Tyr Ala Leu Arg Ser Gln Glu Leu Arg Lys
                300                 305                 310

ACC TTC AAA GAG ATC ATC TCT TCC TAT CCC CTG GGA GGC CTT TGT GAC     1374
Thr Phe Lys Glu Ile Ile Ser Ser Tyr Pro Leu Gly Gly Leu Cys Asp
            315                 320                 325

TTG TCT AGC AGA TAT TAAATGGGGA CAGAGCACGC AATATAGGAA CATCCATAAG     1429
Leu Ser Ser Arg Tyr
        330

AGACTTTTTC ACTCTTACCC TACCTGAATA TTCTACTTCT GCAACAGCTT TCTCTTCCGT   1489

GTAGGGTACT GGTTGAGATA TCCATTGTGT AAATTTAAGC CTATGATTTT TAATGAGAAA   1549

AAATGCCCAG TCTCTGTATT ATTTCCAATC TCATGCTACT TTTTTGGCCA TAAAATATGA   1609

ATCTATGTTA TAGGTTGTAG GCACTGTGGA TTTACAAAAA GAAAAGTCCT TATTAAAAGC   1669

TT                                                                  1671
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Fig. 2

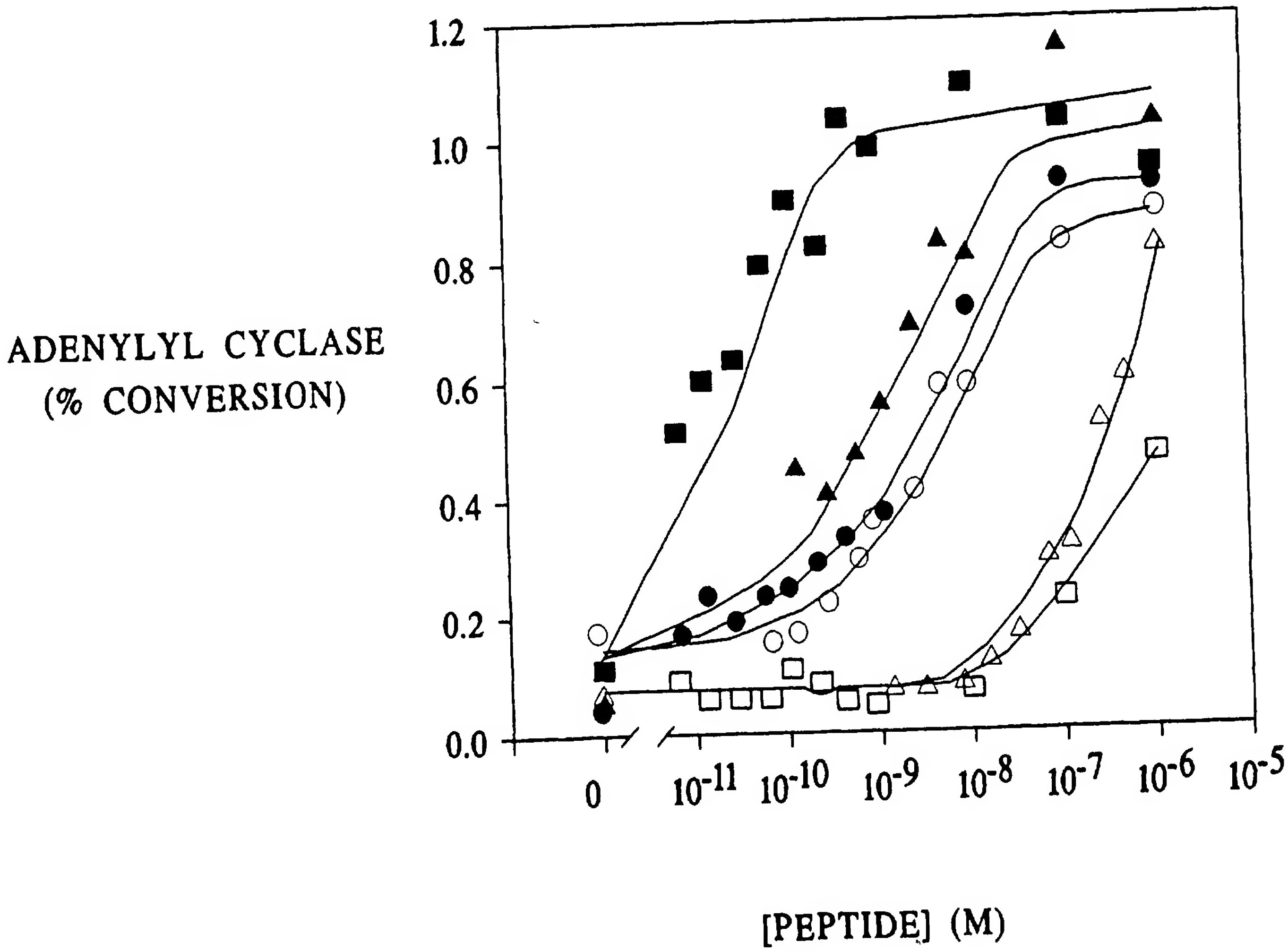

ADENYLYL CYCLASE
(% CONVERSION)
1.2
1.0
0.8
0.6
0.4
0.2
0.0
0
10^{-11}
10^{-10}
10^{-9}
10^{-8}
10^{-7}
10^{-6}
10^{-5}
[PEPTIDE] (M)

Fig. 3

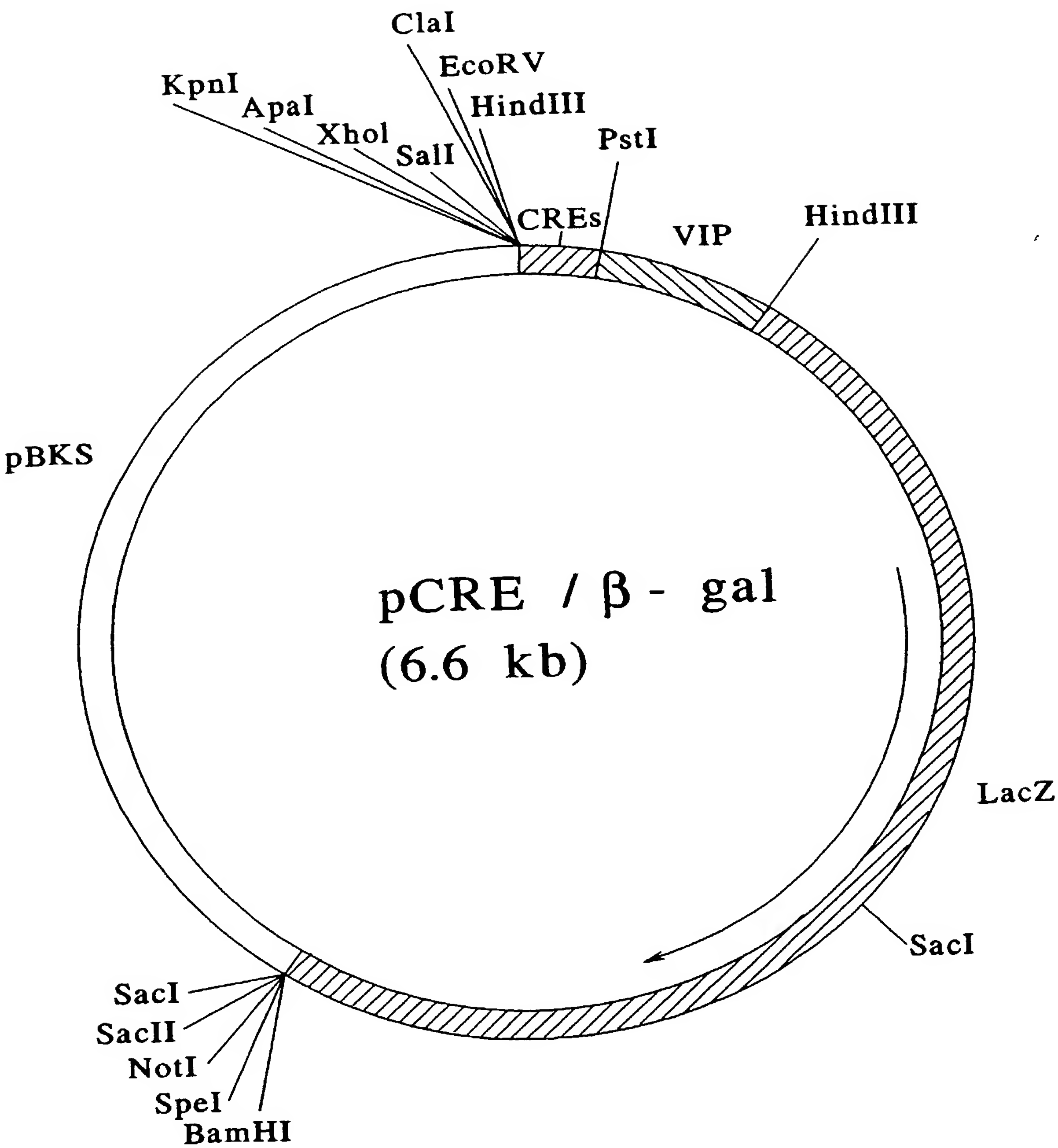
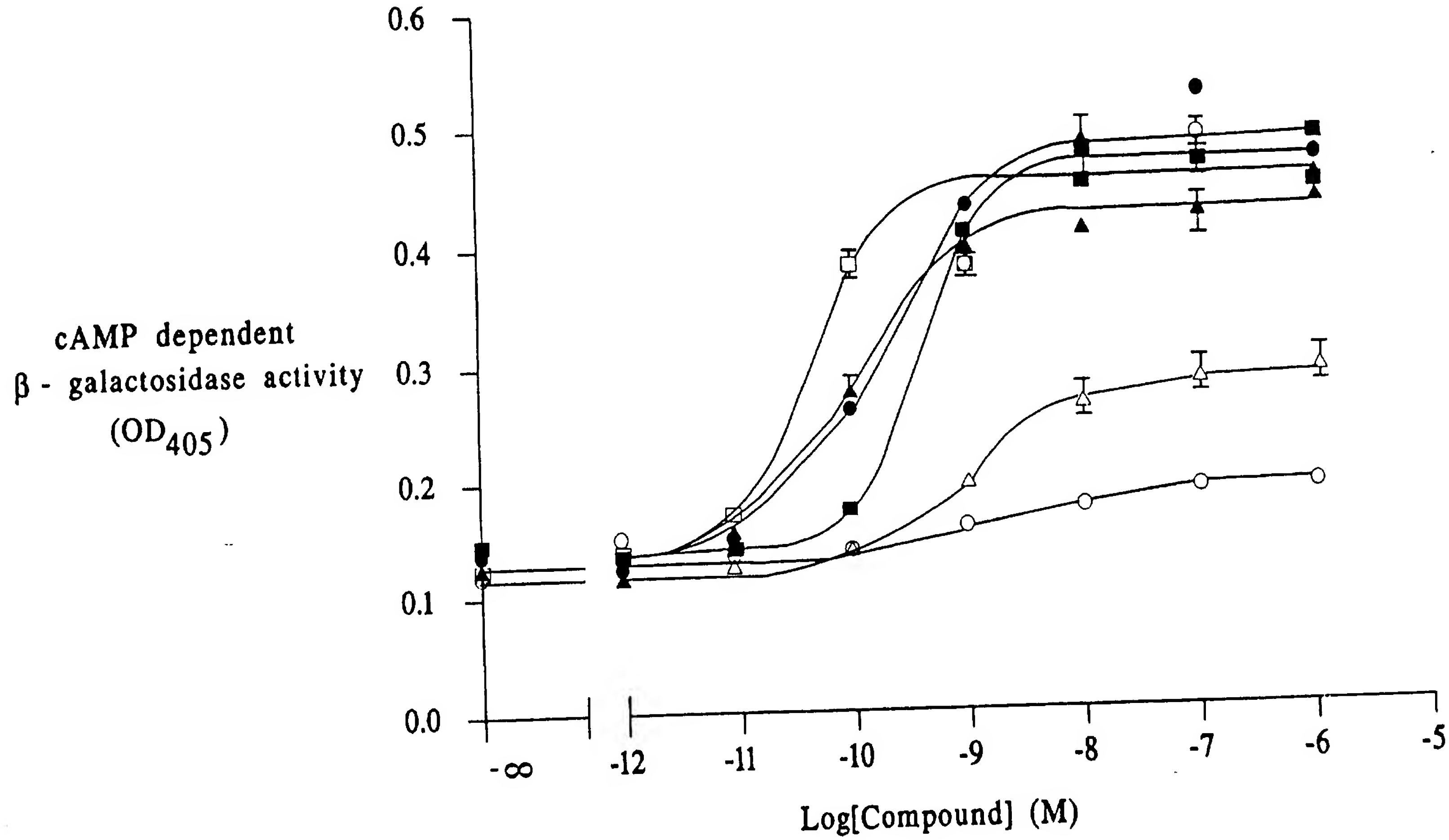
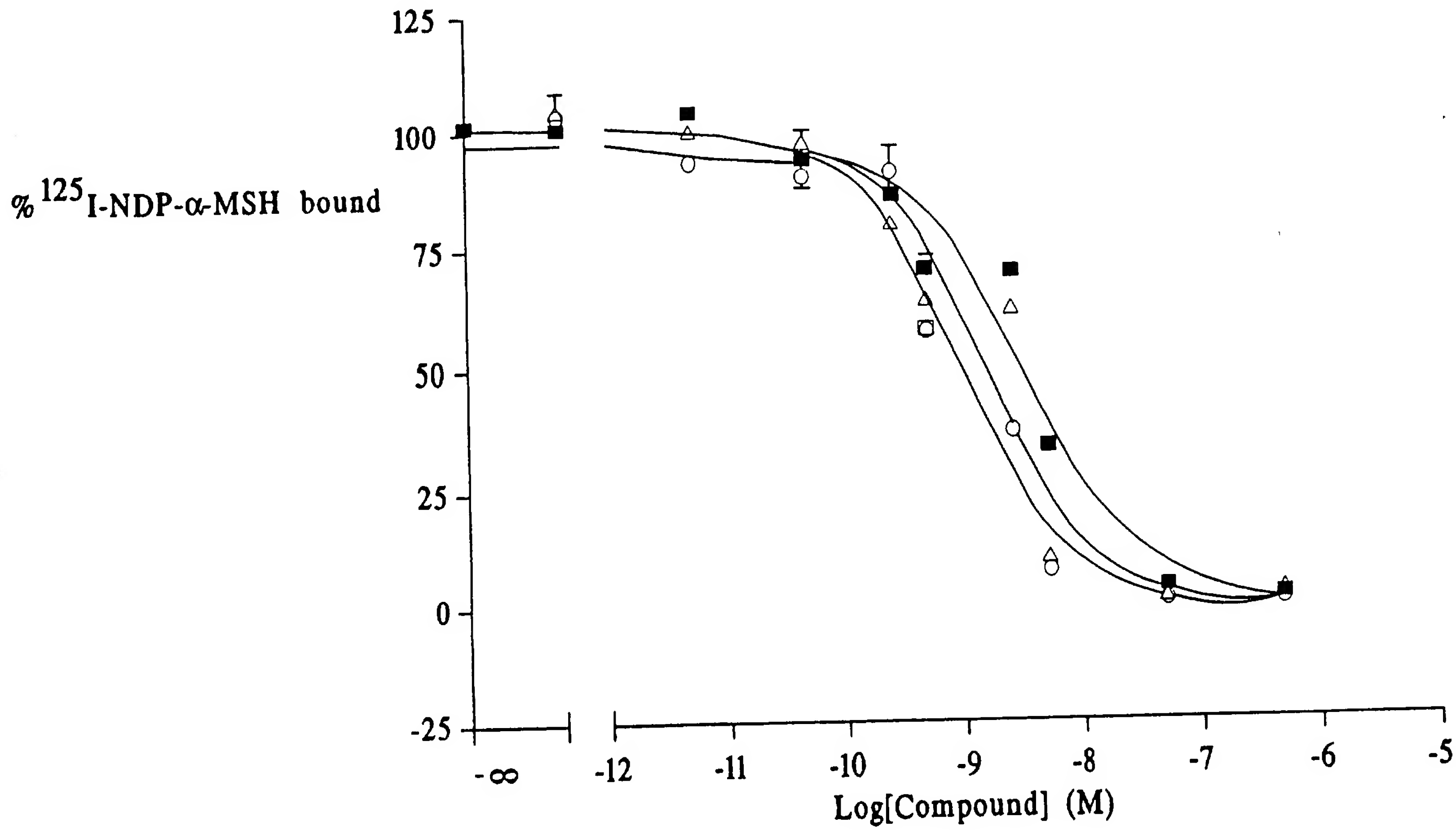

ClaI
EcoRV
KpnI
ApaI
XhoI
HindIII
SalI
PstI
CREs
VIP
HindIII
pBKS
pCRE / β - gal
(6.6 kb)
LacZ
SacI
SacI
SacII
NotI
SpeI
BamHI

Fig. 4


cAMP dependent
β - galactosidase activity
(OD405)
0.6
0.5
0.4
0.3
0.2
0.1
0.0
-∞
-12
-11
-10
-9
-8
-7
-6
-5
Log[Compound] (M)

hMC4-R

Fig. 5


125
100
75
50
25
0
-25
% ^{125}I-NDP-α-MSH bound
-∞
-12
-11
-10
-9
-8
-7
-6
-5
Log[Compound] (M)

hMC4-R

Fig. 6

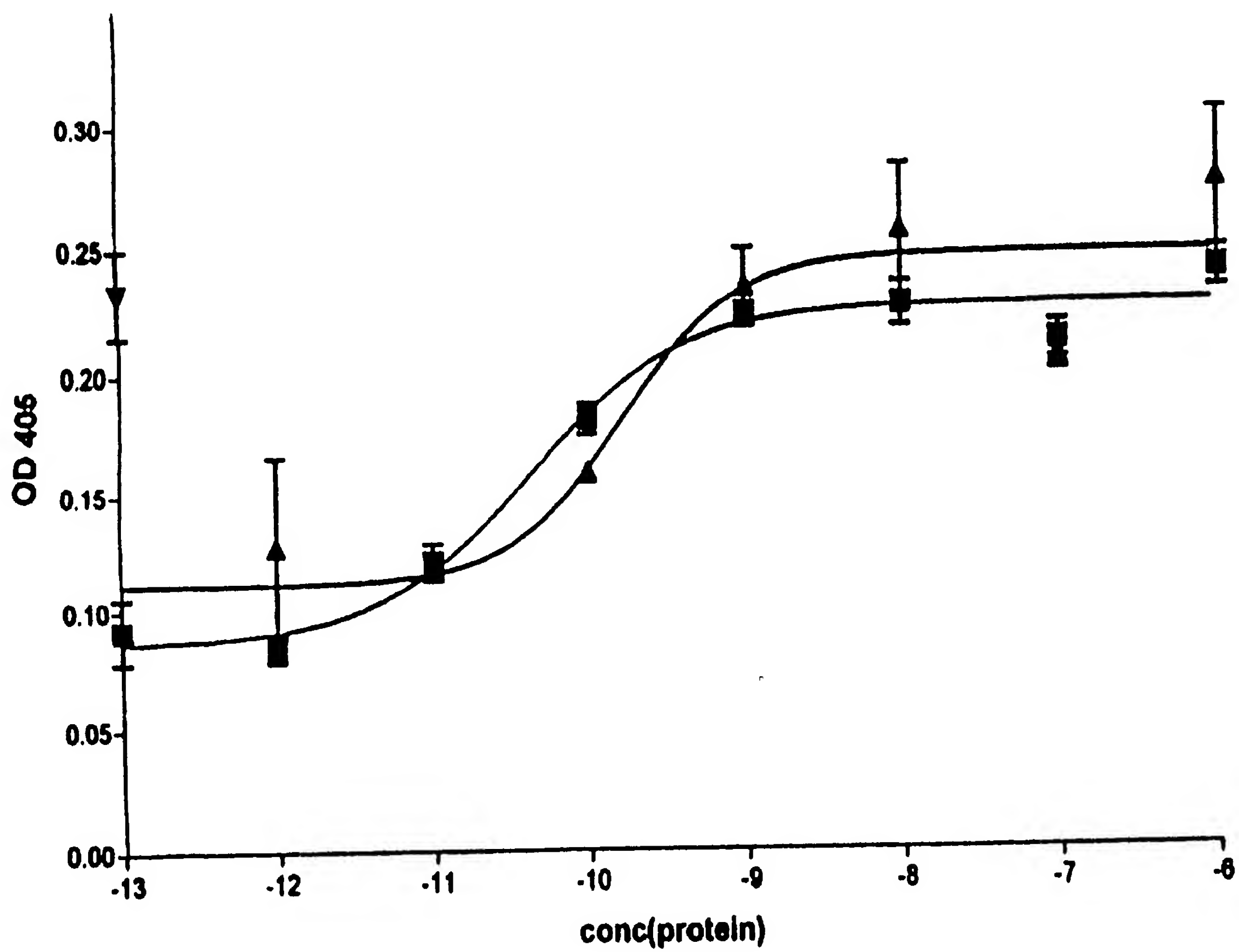


Fig. 7A

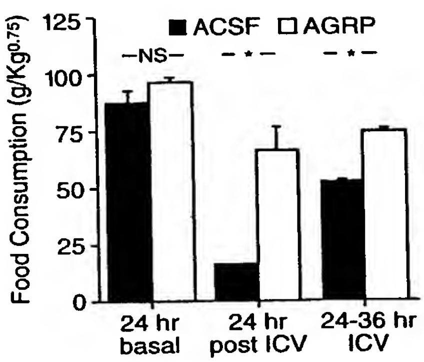
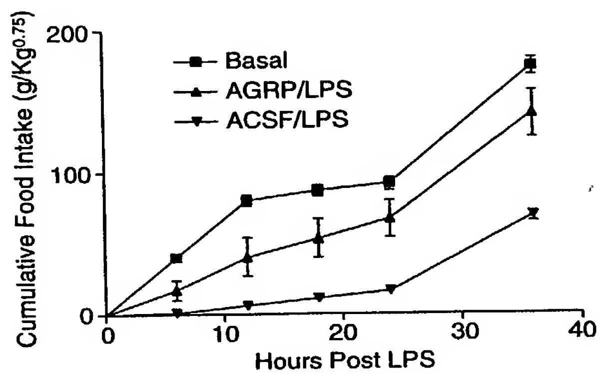


Fig. 7B



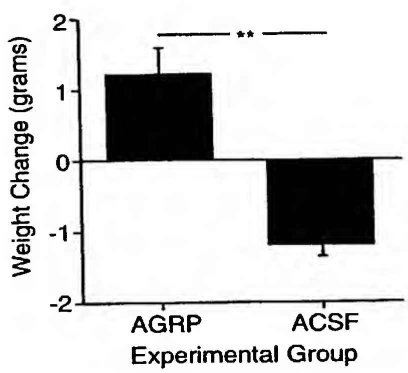


Fig. 7C

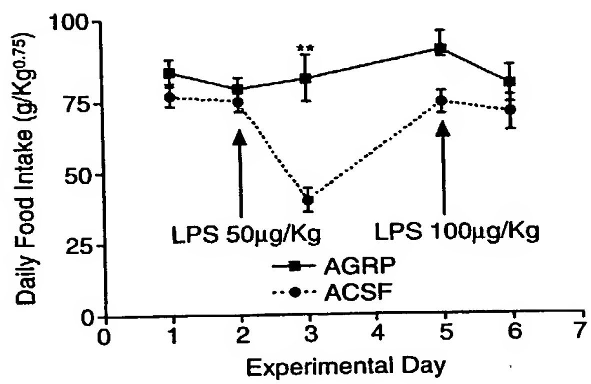


Fig. 7D

Fig. 8A

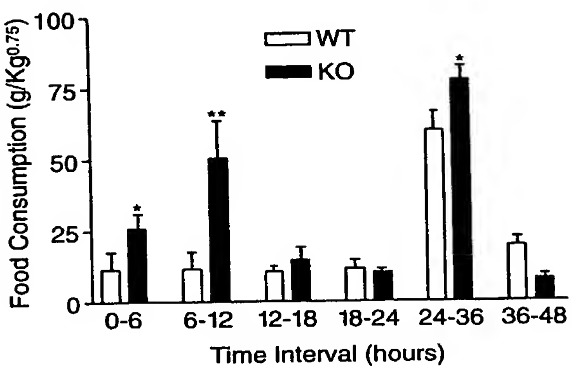
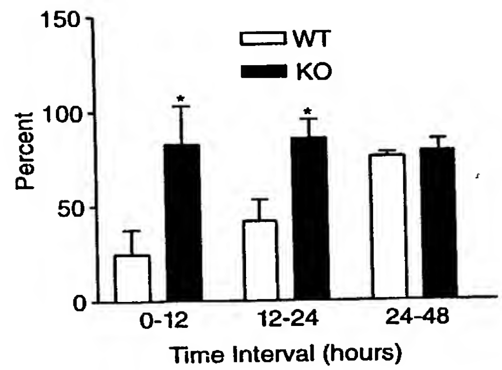


Fig. 8B



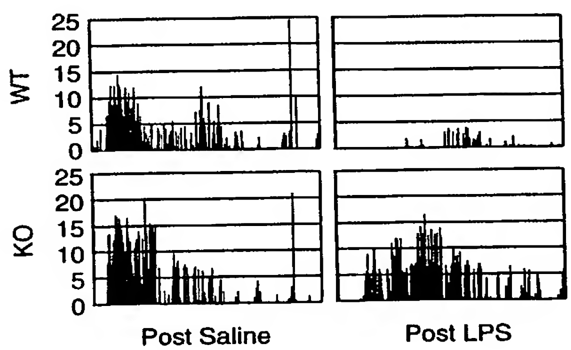


Fig. 8C

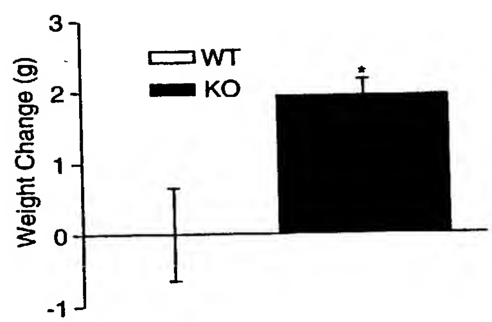


Fig. 8D

Adrenal Stress Response to LPS in MC4-RKO Mice

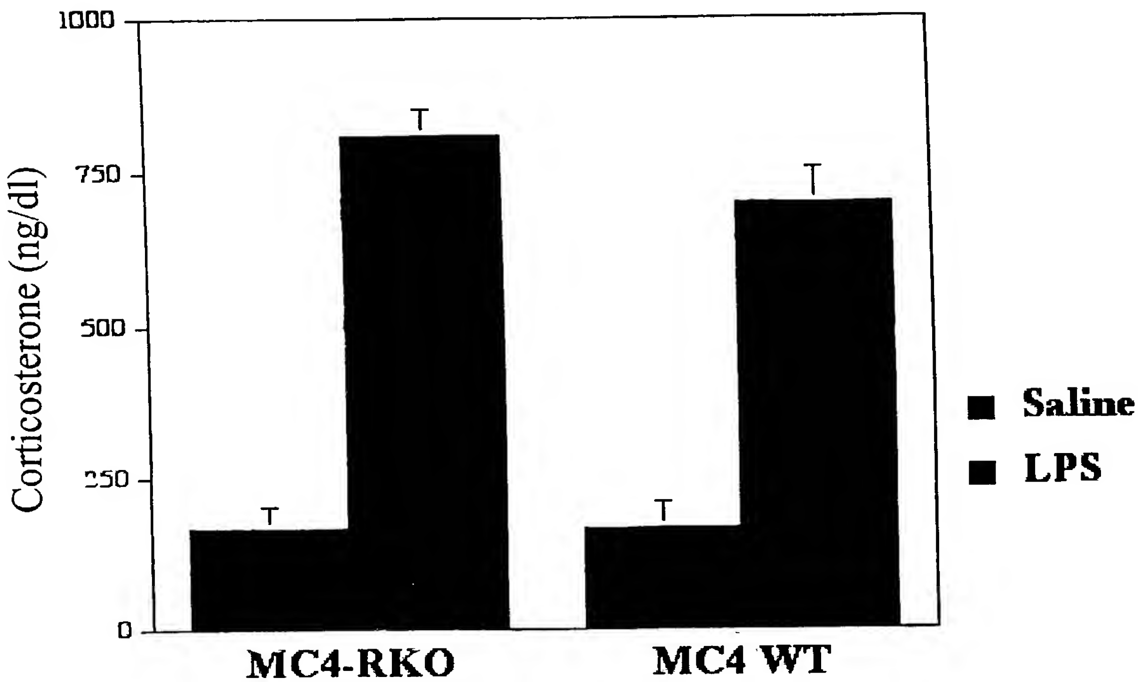


Fig. 8E

Fig. 9A

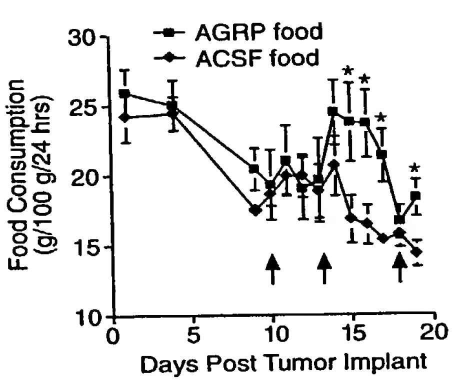
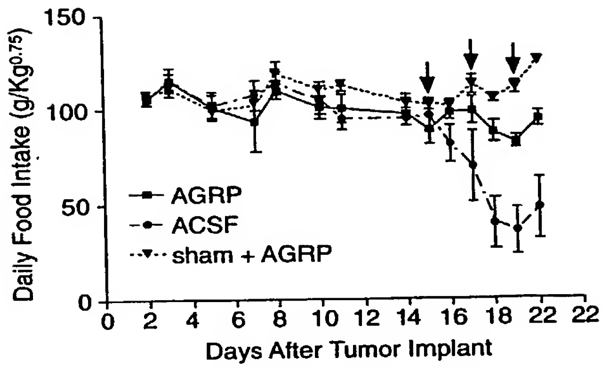


Fig. 9B



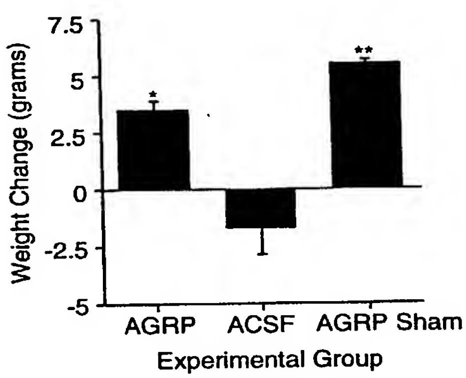


Fig. 9C

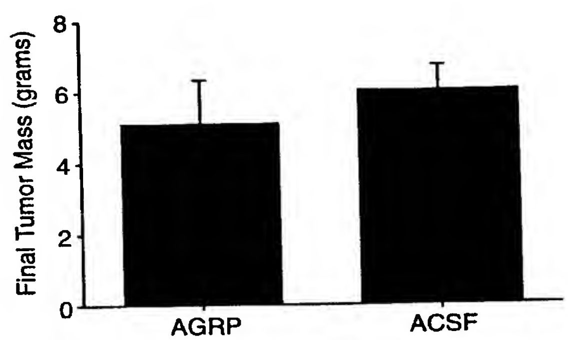


Fig. 9D

Fig. 10A

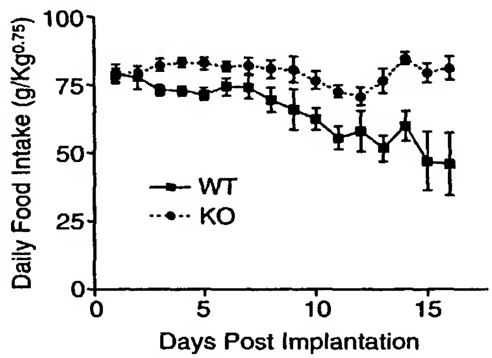
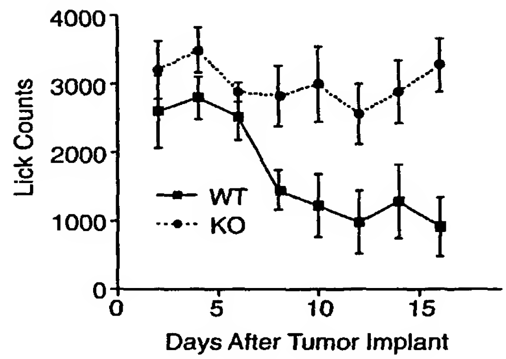


Fig. 10B



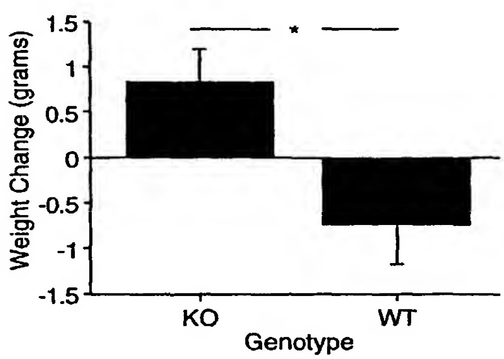


Fig. 10C

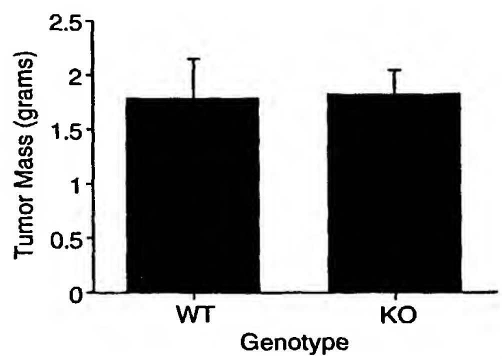


Fig. 10D

Carcass Weight Change During Tumor Growth

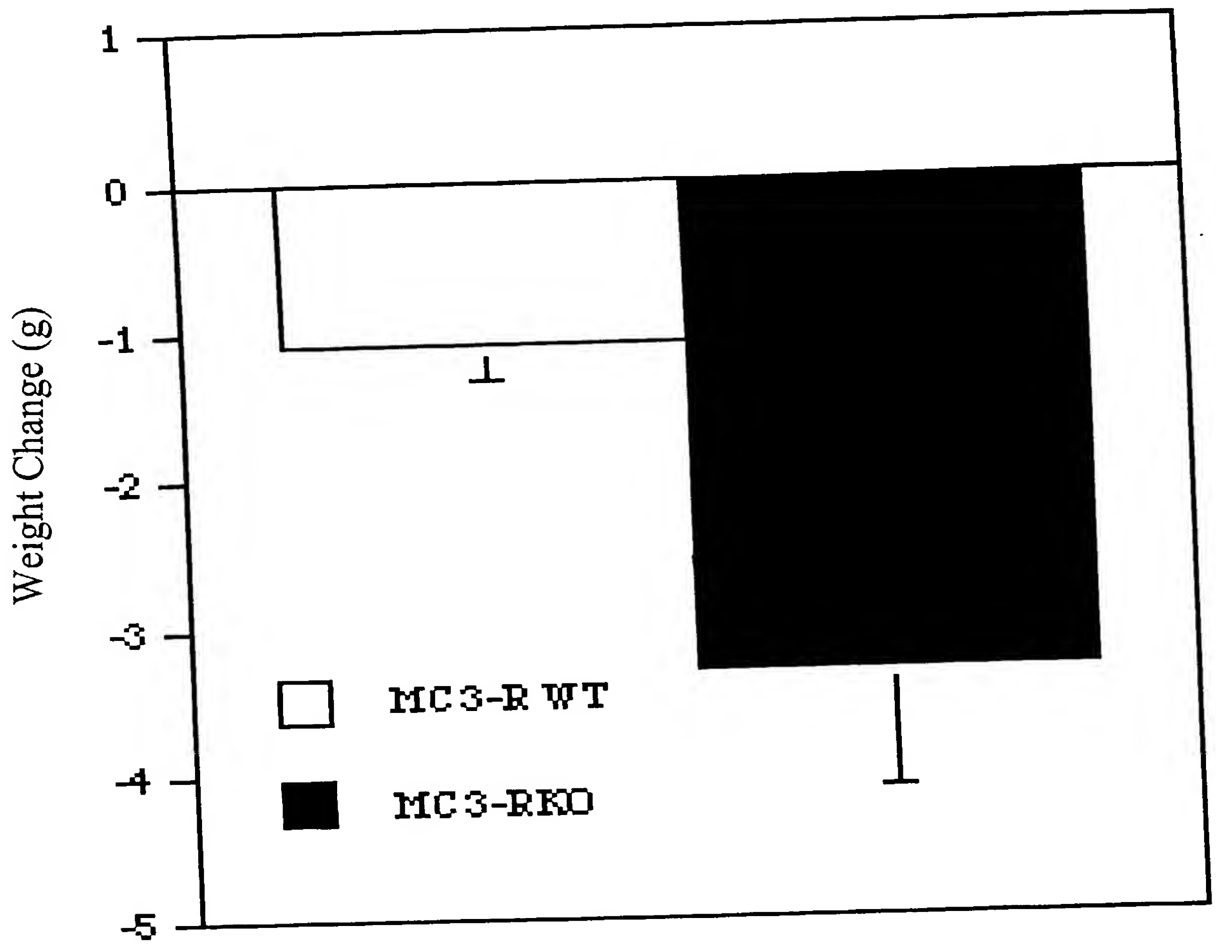
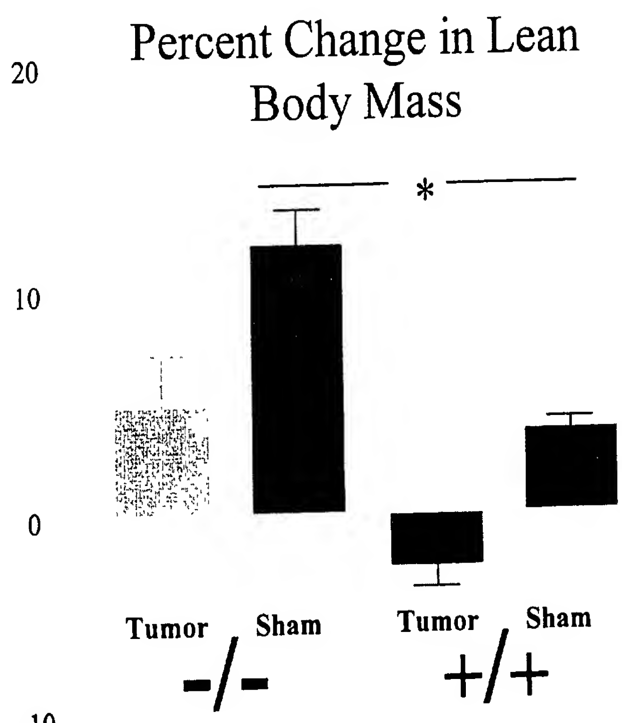


Fig. 10E

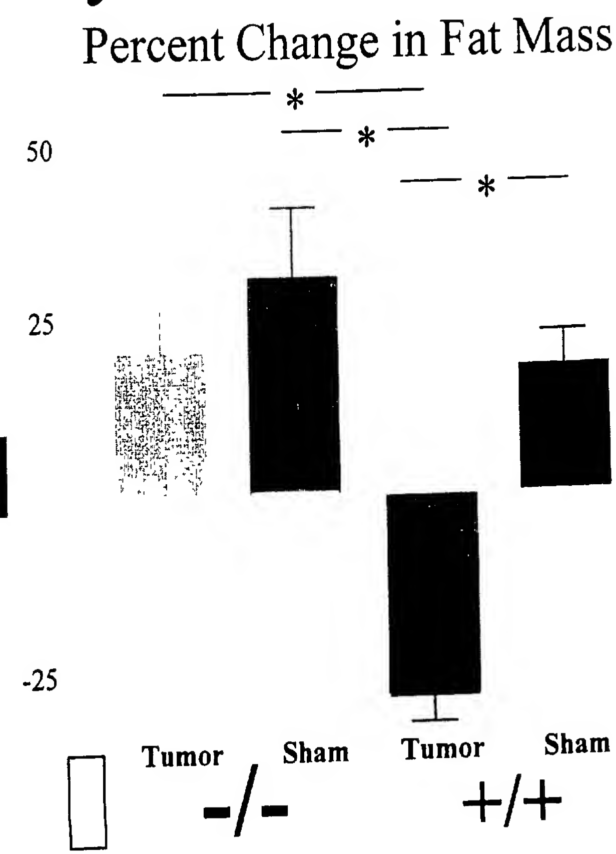
DEXA Body Composition Analysis

Fig. 11A



ANOVA p<0.005. *p<0.01 post hoc

Fig. 11B



Metabolic Response to LPS in MC4-RKO Mice

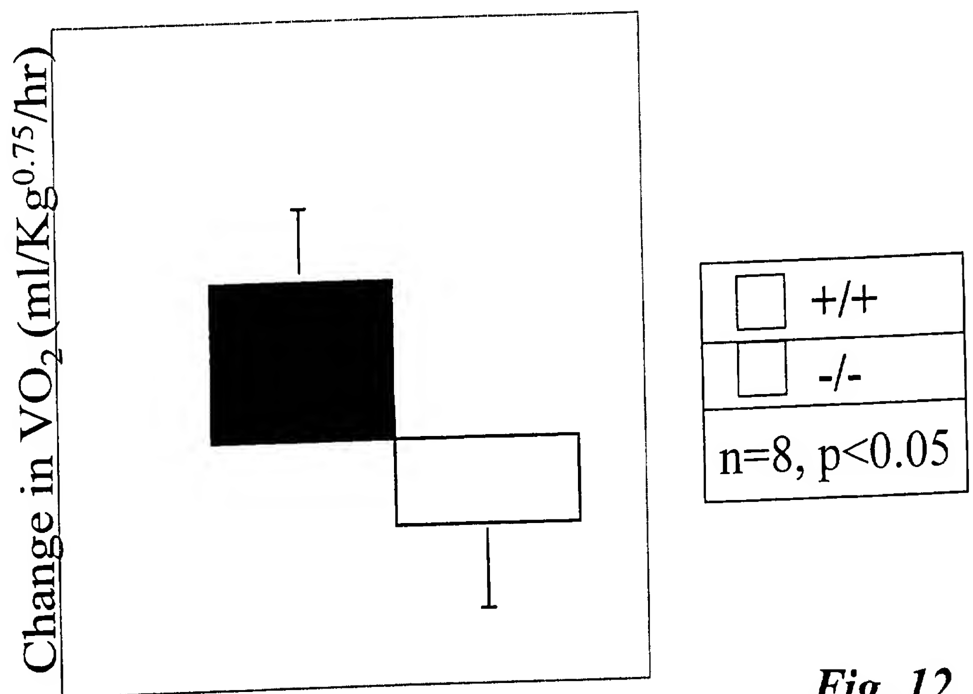


Fig. 12